10621670

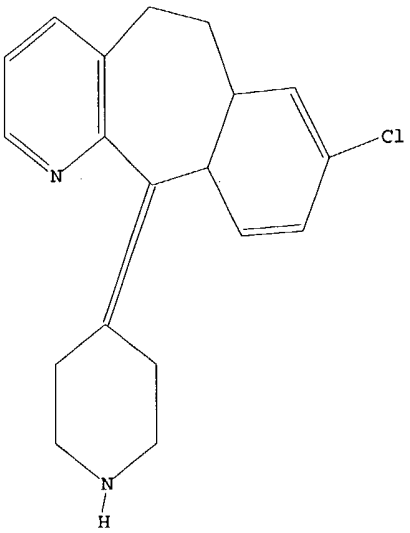
> d his

(FILE 'HOME' ENTERED AT 18:41:35 ON 28 JUN 2004)

FILE 'REGISTRY' ENTERED AT 18:41:50 ON 28 JUN 2004
L1 STRUCTURE UPLOADED
L2 2 S L1
L3 STRUCTURE UPLOADED
L4 1 S L3
L5 33 S L3 SSS FULL

FILE 'CAPLUS' ENTERED AT 18:48:39 ON 28 JUN 2004
L6 260 S L5
L7 9 S L6 AND (HEMIFURMAR? OR FUMAR?)
L8 124 S HEMIFUMARATE
L9 1 S L6 AND L8
L10 8 S L7 NOT L9
L11 659 S LORATADIN?
L12 0 S L8 AND L11
L13 37 S L8 AND FUMAR?
L14 19 S L8 (P) FUMAR?
L15 0 S L14 AND ALLERG?
L16 0 S L14 AND ANTIHISTAMIN?

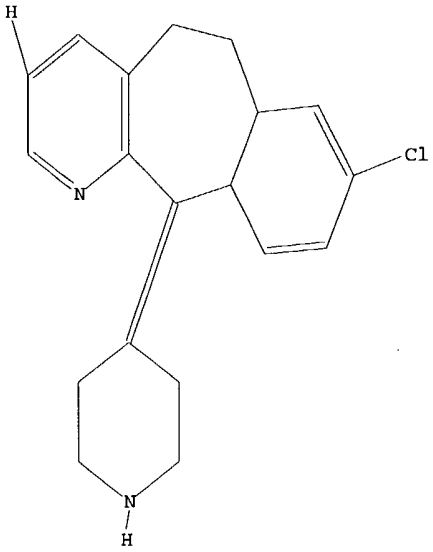
=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> d l3
L3 HAS NO ANSWERS
L3 STR

10621670

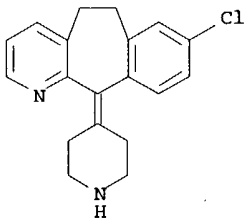


10621670

L7 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:392073 CAPLUS
DN 140:395532
TI Antihistamine and decongestant oral dosage forms
IN Kositprapa, Unchalee; Sriwongjanya, Mongkol
PA USA
SO U.S. Pat. Appl. Publ., 10 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004091533	A1	20040513	US 2002-291103	20021108
PRAI US 2002-291103		20021108		

AB The present invention relates to an oral pharmaceutical formulation that employs: (1) a compressed core containing a decongestant or pharmaceutically acceptable salt thereof; (2) a delayed release coating on the compressed core; and (3) immediate release therapeutic amts. of a decongestant and an antihistamine. For example, a core tablet containing pseudoephedrine was coated with a delayed release composition containing Euidragit S100, followed by (1) an immediate release coating composition containing pseudoephedrine sulfate, (2) a seal coating containing Opadry clear, (3) loratadine immediate release coating, and (4) seal coating containing Opadry clear.
IT **100643-71-8**, Descarboethoxy loratadine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled-release oral dosage forms of antihistamine and decongestant)
RN 100643-71-8 CAPLUS
CN 5H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



L7 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:267177 CAPLUS
DN 140:276210
TI Drug delivery devices containing neuraminidase inhibitor and an H1 antagonist
IN Faour, Joaquina; Vergez, Juan A.; Ricci, Marcelo A.
PA Argent.
SO U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of WO 2004 19,917.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004062801	A1	20040401	US 2003-619720	20030715
US 2003044457	A1	20030306	US 2001-907486	20010717
US 6605302	B2	20030812		
WO 2004019917	A1	20040311	WO 2002-CR5	20020829

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-907486	A2	20010717		
WO 2002-CR5	A2	20020829		

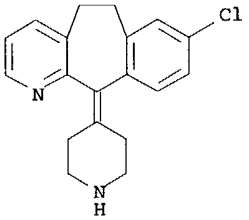
10621670

AB The present invention provides a dual release solid dosage form containing a first composition that releases a neuraminidase inhibitor, such as oseltamivir, zanamivir, or peramivir, in a controlled manner and a second composition that releases an H1 antagonist in a rapid and/or immediate manner. A wide range of H1 antagonist antihistamines, especially fexofenadine and loratadine, can be used in this device. Particular embodiments of the invention provide osmotic devices having predetd. release profiles. The device is useful for the treatment of respiratory congestion and other viral infection associated symptoms. For example, osmotic device tablets containing oseltamivir phosphate and fexofenadine hydrochloride were prepared

IT **100643-71-8**, Desloratadine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled-release drug delivery device containing neuraminidase inhibitor and H1 antagonist)

RN 100643-71-8 CAPLUS

CN 5H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



L7 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:171546 CAPLUS

TI High-performance liquid chromatographic method for the bioequivalence evaluation of desloratadine **fumarate** tablets in dogs

AU Liu, Lihe; Qi, Meiling; Wang, Peng; Li, Haozhi

CS School of Pharmacy, Shenyang Pharmaceutical University, Shenyang, Peop. Rep. China

SO Journal of Pharmaceutical and Biomedical Analysis (2004), 34(5), 1013-1019
CODEN: JPBADA; ISSN: 0731-7085

PB Elsevier Science B.V.

DT Journal

LA English

AB A simple HPLC method was developed for the determination of desloratadine in dog blood plasma and was used for evaluating the bioequivalence of desloratadine **fumarate** tablets and desloratadine tablets in dogs. Chromatog. separation was performed on a Hypersil CN column (150 mm+5.0 mm, 5 μm) using a mixture of MeOH, acetonitrile and phosphate buffer (pH 5.5; 0.01 mol/L) (35:35:30) as mobile phase delivered at a flow rate of 0.8 mL/min. The detection was set at 241 nm. The limit of quantitation was 5.0 ng/mL. The calibration range was from 5.0 to 800.0 ng/mL. Inter- and intra-day precision ranged 1.8-3.8% and 2.2-9.0%, resp. The recovery of desloratadine from dog plasma ranged 78.8-82.0%. The developed method was applied to the bioequivalence studies of desloratadine **fumarate** tablets (test preparation) and desloratadine tablets (reference preparation) in 5 dogs. Pharmacokinetic parameters tmax, Cmax, AUC0-t, AUC0-∞, t1/2 were determined from plasma concentration-time profiles of both prepns. The anal. of variance (ANOVA) did not show any significant difference between the 2 prepns. and 90% confidence intervals fell within the acceptable range for bioequivalence. Based on these statistical inferences, it was concluded that the 2 prepns. exhibited comparable pharmacokinetic profiles and that desloratadine **fumarate** tablets was bioequivalent to desloratadine tablets.

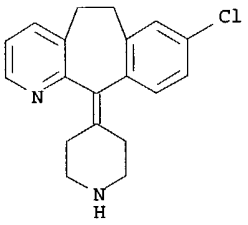
IT INDEXING IN PROGRESS

IT **100643-71-8**, Desloratadine
RL: ANT (Analyte); PKT (Pharmacokinetics); ANST (Analytical study); BIOL (Biological study)
(bioequivalence evaluation of desloratadine **fumarate** tablets in dogs with HPLC)

RN 100643-71-8 CAPLUS

CN 5H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-piperidinylidene)- (9CI) (CA INDEX NAME)

10621670



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:120725 CAPLUS
DN 140:169678
TI Novel salt and polymorphs of desloratadine hemifumarate
IN Ray, Anup Kumar; Patel, Hiren V.; Patel, Mahendra R.
PA Geneva Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004012738	A1	20040212	WO 2003-US22312	20030717
US 2004058949	A1	20040325	US 2003-621670	20030717

PI WO 2004012738 A1 20040212 WO 2003-US22312 20030717
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004058949 A1 20040325 US 2003-621670 20030717
PRAI US 2002-401153P P 20020805

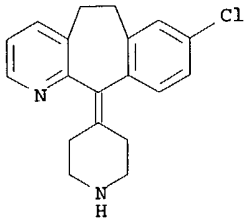
AB This invention provides a process of preparation of polymorphic forms of desloratadine hemifumarate salts that show much higher solubility in water and also in protic organic solvents compared to the parent desloratadine. The process of preparing the polymorphic forms comprising: (a) mixing the ethanolic solution of desloratadine and **fumaric** acid at a temperature of about 55° to 70°, and stirring for 30 to 45 min after mixing, and thereafter filtering the solid thereby prepared in hot condition; to yield the polymorphic Form 2 having a DSC of 232° ± 2°; or (b) mixing the ethanolic solution of desloratadine and **fumaric** acid at a temperature of about 15° to room temperature (25°) and stirring at this temperature for 30 to 45 min, then filtering at room temperature; to yield the polymorphic Form 1 having a DSC of 224° ± 2°. A pharmaceutical composition comprises an antiallergic effective amount of either Form 1 or Form 2 of desloratadine hemifumarate and a pharmaceutically acceptable carrier.

IT **656253-72-4P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polymorphs of desloratadine hemifumarate for dosage forms)
RN 656253-72-4 CAPLUS
CN 5H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-piperidinylidene)-, (2E)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 100643-71-8
CMF C19 H19 Cl N2

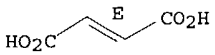
10621670



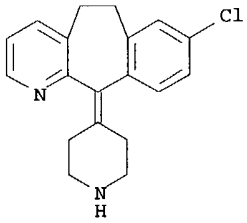
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



IT **100643-71-8**, Desloratadine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of polymorphs of desloratadine hemifumarate for dosage forms)
RN 100643-71-8 CAPLUS
CN 5H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



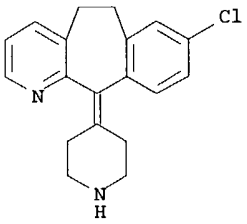
L7 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:988191 CAPLUS
DN 140:12688
TI Comparison of ketotifen **fumarate** ophthalmic solution alone, desloratadine alone, and their combination for inhibition of the signs and symptoms of seasonal allergic rhinoconjunctivitis in the conjunctival allergen challenge model: a double-masked, placebo- and active-controlled trial
AU Crampton, H. Jerome
CS Ophthalmic Research Associates, North Andover, MA, USA
SO Clinical Therapeutics (2003), 25(7), 1975-1987
CODEN: CLTHDG; ISSN: 0149-2918
PB Excerpta Medica, Inc.
DT Journal
LA English
AB Background: Ketotifen **fumarate** is a topical antiallergic combination mast-cell stabilizer and antihistamine indicated for the temporary prevention of ocular itching due to allergic conjunctivitis. Desloratadine is a systemic antihistamine indicated for the treatment of seasonal and perennial allergic rhinitis. Objective: The purpose of this study was to compare the efficacy of ketotifen 0.025% ophthalmic solution instilled in the eye, desloratadine 5-mg tablets taken orally, and their combination for prevention of the signs and symptoms of allergic rhinoconjunctivitis, as induced by the conjunctival allergen challenge (CAC) model. Methods: This was a randomized, double-masked, placebo- and active-controlled, single-center clin. trial. At visit 1, the dose of allergen necessary to elicit a qualifying allergic reaction was determined for subjects meeting the entry criteria. At visit 2, the allergen dose determined at visit 1 was confirmed, and all subjects who had a qualifying ocular and nasal allergic reaction were randomized to 1 of 3 treatment groups:

ketotifen ophthalmic solution and placebo tablet, desloratadine tablet and placebo eyedrop, or ketotifen and desloratadine. Subjects were instructed to instill 1 drop into each eye twice daily and take 1 tablet with water once daily at the same time as the morning eyedrop for .apprx.4 wk. At visit 3, subjects brought in their medication and were given 1 drop of the eyedrop bilaterally and 1 tablet with water. Bilateral CAC was performed 2 h after administration of medication. Using standardized scales, subjects rated ocular itching at 3, 5, and 7 min after CAC; ocular tearing and eyelid swelling at 10, 15, and 20 min after CAC; and nasal signs and symptoms (sneezing, rhinorrhea and postnasal drip, pruritus, and nasal congestion) at 10, 20, 30, 40, and 50 min after CAC. The investigator graded ocular redness and chemosis at 10, 15, and 20 min after CAC. At all visits, subjects were offered an anti-allergy eyedrop to relieve any immediate ocular discomfort caused by CAC. Results: One hundred two subjects were screened-82 (55 women, 27 men; mean age, 42.8 yr [range, 21-70 yr]) were randomized to treatment, and 80 completed the study. Subjects in the group that received ketotifen (n = 27) and the group that received ketotifen with desloratadine (n = 26) had significantly lower mean itching scores compared with those in the group that received desloratadine alone (n = 27) at all time points ($P \leq 0.05$). Total ocular redness, calculated by summing the mean redness scores for each of the 3 vessel beds, was significantly lower in the ketotifen group than in the other treatment groups at most time points ($P \leq 0.05$). All treatments attenuated nasal symptoms; no statistically significant differences were noted between treatment groups, with the exception of the 50-min time point, at which combination treatment was significantly more effective than ketotifen alone ($P \leq 0.05$). The proportion of subjects who requested relief drops after CAC was significantly lower in both the ketotifen alone and combination treatment groups compared with the desloratadine alone group ($P = 0.004$). Conclusions: Ketotifen ophthalmic solution significantly decreased the signs and symptoms of ocular and nasal allergic rhinoconjunctivitis. The addition of ketotifen to the oral desloratadine regimen improved the overall antiallergic efficacy of both medications.

IT **100643-71-8**, Desloratadine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of efficacy of ketotifen **fumarate** ophthalmic solution alone, desloratadine alone, and their combination for inhibition of signs and symptoms of seasonal allergic rhinoconjunctivitis in conjunctival allergen challenge model)

RN 100643-71-8 CAPLUS

CN 5H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

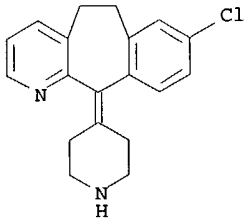
L7 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:720795 CAPLUS
DN 138:280580
TI FDA new drug approvals in 2001
AU Zhao, Kang; He, Lan; Reiner, John
CS The College of Pharmaceuticals and Biotechnology, Tianjin University, Peop. Rep. China
SO Frontiers of Biotechnology & Pharmaceuticals (2002), 3, 400-413
CODEN: FBPRBL
PB Science Press New York Ltd.
DT Journal; General Review
LA English
AB A review covering the 24 new drugs approved by the Food and Drug Administration in the year 2001. Therapeutics are grouped according to the following coded areas: (A) agents affecting neurotransmitters and cytokines, (B) antiinflammatory agents, (C) hormone related agents, (D)

anti-infectious agents, and (E) miscellaneous agents. A synopsis for each drug includes a brief description of its medical utility, a mechanism of action if known, a chemical structure, and a pathway for its synthesis.

IT **100643-71-8P**, Desloratadine
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(FDA new drug approvals in 2001)

RN 100643-71-8 CAPLUS

CN 5H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:503329 CAPLUS

DN 137:68175

TI Texture masked particles coated with a film-forming polymer and an anti-grit agent

IN Parikh, Narendra; McTeigue, Daniel; Wynn, David W.; Pillai, Ravivaj S.

PA McNeil-PPC, Inc., USA

SO Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

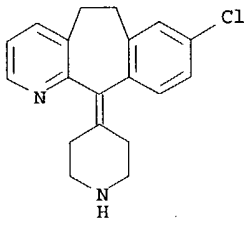
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1219291	A1	20020703	EP 2001-310751	20011221
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2002119196	A1	20020829	US 2000-745243	20001221
	AU 2001097361	A5	20020627	AU 2001-97361	20011221
	CN 1366878	A	20020904	CN 2001-145483	20011221
	JP 2002272817	A2	20020924	JP 2001-390445	20011221
	ZA 2001010547	A	20030730	ZA 2001-10547	20011221
	NZ 516341	A	20030829	NZ 2001-516341	20011221
	BR 2001006912	A	20030916	BR 2001-6912	20011221
PRAI	US 2000-745243	A	20001221		

AB Texture masked particles and chewable tablets made therefrom are disclosed. The texture masked particles are comprised of (i) a core containing an active ingredient, e.g. and antacid or non-steroidal anti-inflammatory agent, (ii) an optional first layer of a taste masking agent that substantially covers the core, and (iii) a texture masking coating layer on the surface of the core comprising a film-forming polymer and an anti-grit agent. A taste masked particles comprise (i) a core containing an active ingredient, and (ii) a taste masking agent composed of an enteric polymer and an insol. film-forming polymer. The particles may be produced into a tablet form, such as a chewable tablet, that provides for the immediate release of the active ingredient. For example, a texture masking coating solution was prepared by dispersing equal amount of hydroxypropyl Me cellulose and polyethylene glycol 800 together with acesulfame potassium (1% of solids) in a solvent comprising 77% ethanol and 23% water so that the solid materials represented 10% of the finished solution Then, Et cellulose-encapsulated acetaminophen (1000 g) was sprayed with the texture masking coating solution prepared so that the level of the texture masking coating materials was 7% by weight of the total finished texture masked coated particles. The resulting coated particles had an average diameter of 380 μ.

IT **100643-71-8**, Desloratadine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(texture and taste masked particles coated with film-forming polymer and anti-grit agent)

10621670

RN 100643-71-8 CAPLUS
CN 5H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:353315 CAPLUS
DN 136:374833
TI Inhalant composition containing tiotropium salts and anti-histamines
IN Pairet, Michel; Pieper, Michael Paul; Meade, Christopher John Montague; Schmelzer, Christel
PA Boehringer Ingelheim Pharma Kg, Germany
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002036163	A2	20020510	WO 2001-EP12510	20011023
	WO 2002036163	A3	20021212		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	DE 10138272	A1	20030227	DE 2001-10138272	20010810
	US 2002151541	A1	20021017	US 2001-7182	20011019
	US 2002183292	A1	20021205	US 2001-86145	20011019
	AU 2002014030	A5	20020515	AU 2002-14030	20011023
	EP 1341538	A2	20030910	EP 2001-982446	20011023
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004512379	T2	20040422	JP 2002-538972	20011023
	US 2002137764	A1	20020926	US 2001-40196	20011025
	US 2003181478	A1	20030925	US 2003-395777	20030324
PRAI	DE 2000-10054042	A	20001031		
	DE 2001-10138272	A	20010810		
	US 2000-253613P	P	20001128		
	DE 2000-10062712	A	20001215		
	US 2000-257220P	P	20001221		
	US 2001-314599P	P	20010824		
	WO 2001-EP12510	W	20011023		
	US 2001-40196	B1	20011025		

AB The invention relates to inhalant compns. based on tiotropium salts and anti-histamines, a method for their production and their use for treating respiratory illnesses, e.g. allergic and non-allergic rhinitis. Thus and inhalation powder contained per microcapsule (μg): tiotropium bromide 21.7; epinastine-hydrochloride 200; lactose 4778.3.
IT **100643-71-8**, Desloratadine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhalant composition containing tiotropium salts and anti-histamines)
RN 100643-71-8 CAPLUS
CN 5H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-piperidinylidene)- (9CI) (CA INDEX NAME)

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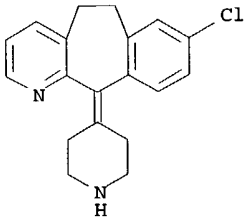

L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:635179 CAPLUS
DN 125:275664
TI 8-Chloro-11-[1-[(5-methyl-3-pyridyl)methyl]-4-piperidylidene]-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridine **fumarate** and its preparation and use as a PAF antagonist and antihistaminic
IN Carceller, Elena; Recasens, Nuria; Almansa, Carmen; Bartroli, Javier; Merlos, Manel; Giral, Marta
PA J. Uriach & Cia. S.A., Spain
SO Span., 11 pp.
CODEN: SPXXAD
DT Patent
LA Spanish
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	ES 2087818	A1	19960716	ES 1993-2460	19931124
	ES 2087818	B1	19970316		
	NO 9404487	A	19950526	NO 1994-4487	19941123
PRAI	ES 1993-2460		19931124		

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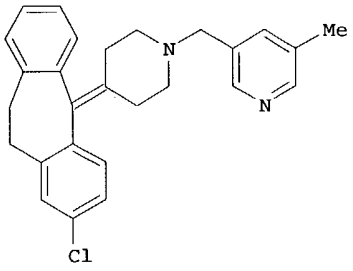
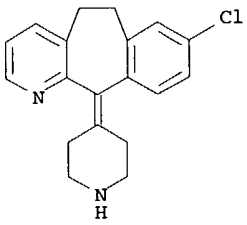


I

AB The title salt I-**fumarate** is prepared for use as an antagonist of PAF (platelet activating factor) and an antihistaminic (no data). I-**fumarate** has improved hygroscopicity and light stability in comparison to I.3HCl or the free base I. For example, I was prepared from loratadine by a sequence of: hydrolytic removal of the N-ethoxycarbonyl group (84%), N-acylation with 5-methylnicotinic acid using DCC and HOBt (65%), and chlorination/reduction of the amide using POCl3 followed by NaBH4 (72%). Treatment of I with **fumaric** acid in EtOH gave 70% I-**fumarate**. When exposed to 98% humidity for 24 h, H2O contents were 5.7% for I, and 28.3% for I.3HCl, but only 0.29% for I-**fumarate**. Similarly, irradiation at 150 klx for 1 h reduced purities to 92.7% for I, to 74% for I.3HCl, but only to 99.2% for I. **fumarate**.

IT **100643-71-8P**, 8-Chloro-11-(4-piperidylidene)-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridine
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of benzocycloheptapyridine derivative **fumarate** salt as PAF antagonist and antihistaminic with improved properties)
RN 100643-71-8 CAPLUS
CN 5H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-piperidinylidene)- (9CI) (CA INDEX NAME)

10621670



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L14 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:369117 CAPLUS
DN 131:26003
TI 2-Aminopyrimidine-fumaric acid cocrystal
AU Goswami, Shyamaprosad; Mahapatra, Ajit Kumar; Nigam, Gur Dayal; Chinnakali, Kandasamy; Fun, Hoong-Kun; Razak, Ibrahim Abdul
CS Department of Chemistry, Bengal Engineering College (Deemed University), Howrah, 711 103, India
SO Acta Crystallographica, Section C: Crystal Structure Communications (1999), C55(4), 583-585
CODEN: ACSCEE; ISSN: 0108-2701
PB Munksgaard International Publishers Ltd.
DT Journal
LA English
AB In crystals of the title compound, 2-aminopyrimidin-1-ium **hemifumarate** hemifumaric acid, C4H6N3+·0.5C4H2O42-·0.5C4H4O4, the asym. unit contains one 2-aminopyrimidine cation, C4H6N3+, protonated at a pyrimidine ring-N atom, 1/2-mol. of **fumaric** acid, C4H4O4, and 1/2 of a **fumarate** ion, C4H2O42-. These are linked by N-H···O, O-H···O and relatively strong C-H···O bonds, resulting in eight- and nine-membered H-bonded rings and an extended supramol. structure. Crystallog. data are given.
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB In crystals of the title compound, 2-aminopyrimidin-1-ium **hemifumarate** hemifumaric acid, C4H6N3+·0.5C4H2O42-·0.5C4H4O4, the asym. unit contains one 2-aminopyrimidine cation, C4H6N3+, protonated at a pyrimidine ring-N atom, 1/2-mol. of **fumaric** acid, C4H4O4, and 1/2 of a **fumarate** ion, C4H2O42-. These are linked by N-H···O, O-H···O and relatively strong C-H···O bonds, resulting in eight- and nine-membered H-bonded rings and an extended supramol. structure. Crystallog. data are given.

L14 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:317796 CAPLUS
DN 126:297699
TI Preparation of crystalline salts of antidopaminergic 2,3,4,5-tetrahydro-1H-3-benzazepine compounds
IN Hansen, Louis Brammer; Amsler, Rolf Emil; Mcgraw, Scott Eugene
PA Novo Nordisk A/s, Den.; Hansen, Louis Brammer; Amsler, Rolf Emil; Mcgraw, Scott Eugene
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9710239	A1	19970320	WO 1996-DK383	19960912
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
	AU 9669235	A1	19970401	AU 1996-69235	19960912
	AU 700596	B2	19990107		
	EP 850237	A1	19980701	EP 1996-930028	19960912
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1200121	A	19981125	CN 1996-197660	19960912
	BR 9610162	A	19990105	BR 1996-10162	19960912
	JP 11512403	T2	19991026	JP 1996-511574	19960912
	NO 9801135	A	19980313	NO 1998-1135	19980313
PRAI	DK 1995-1030		19950915		
	WO 1996-DK383		19960912		

AB Crystalline salts with reproducible crystalline forms and increased solubility were prepared from the antidopaminergic agent, (S)-(+)-8-chloro-5-(5,6-dichloro-2,3-dihydrobenzofuran-7-yl)-3-methyl-2,3,4,5-tetrahydro-1H-3-benzazepin-7-ol (I). Thus, **fumaric** acid was added to I in 99% EtOH at 70°, the solution was cooled to 0°, then filtered to give the **hemifumarate.**
AB Crystalline salts with reproducible crystalline forms and increased solubility were

prepared from the antidopaminergic agent, (S)-(+)-8-chloro-5-(5,6-dichloro-2,3-dihydrobenzofuran-7-yl)-3-methyl-2,3,4,5-tetrahydro-1H-3-benzazepin-7-ol (I). Thus, **fumaric** acid was added to I in 99% EtOH at 70°, the solution was cooled to 0°, then filtered to give the **hemifumarate.**

L14 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:995029 CAPLUS
DN 124:117356
TI Preparation of acid addition salts of (S)-8-chloro-5-(5-bromo-2,3-dihydrobenzofuran-7-yl)-3-methyl-2,3,4,5-tetrahydro-1H-3-benzazepine-7-ol.
IN Hansen, Louis Brammer; Amsler, Rolf Emil; McGraw, Scott Eugene
PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9525102	A1	19950921	WO 1995-DK106	19950308
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TT, UA, UG, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9519454	A1	19951003	AU 1995-19454	19950308
	EP 750616	A1	19970102	EP 1995-912143	19950308
	EP 750616	B1	20010530		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09510222	T2	19971014	JP 1995-523785	19950308
	ES 2158094	T3	20010901	ES 1995-912143	19950308
	US 5658899	A	19970819	US 1995-404394	19950314
PRAI	DK 1994-311	A	19940316		
	WO 1995-DK106	W	19950308		

AB Crystalline salts of (S)-8-chloro-5-(5-bromo-2,3-dihydrobenzofuran-7-yl)-3-methyl-2,3,4,5-tetrahydro-1H-3-benzazepine-7-ol (I) with **fumaric** , L-tartaric, and D-mandelic acids were prepared Thus, **fumaric** acid and I were added to refluxing EtOH and the solution was cooled to room temperature to give 66% I.**hemifumarate.** Pharmaceutical compns. containing I salts are claimed for use in treating dysfunctions of the dopamine D1 receptor system and disorders related to schizophrenia.

AB Crystalline salts of (S)-8-chloro-5-(5-bromo-2,3-dihydrobenzofuran-7-yl)-3-methyl-2,3,4,5-tetrahydro-1H-3-benzazepine-7-ol (I) with **fumaric** , L-tartaric, and D-mandelic acids were prepared Thus, **fumaric** acid and I were added to refluxing EtOH and the solution was cooled to room temperature to give 66% I.**hemifumarate.** Pharmaceutical compns. containing I salts are claimed for use in treating dysfunctions of the dopamine D1 receptor system and disorders related to schizophrenia.

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L14 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:120514 CAPLUS
DN 122:55666
TI Synthesis of radiolabeled racemic and enantiomeric antiarrhythmic agents
AU Stolle, Wayne T.; Stelzer, Lindsay S.; Hester, Jackson B.; Perricone, Salvatore C.; Hsi, Richard S. P.
CS Upjohn Lab., The Upjohn Co., Kalamazoo, MI, 49001, USA
SO Journal of Labelled Compounds and Radiopharmaceuticals (1994), 34(10), 929-42
CODEN: JLCRD4; ISSN: 0362-4803
DT Journal
LA English
AB Ibutilide **fumarate**, racemic N-[4-[4-(ethyl-n-heptylamino)-1-hydroxybutyl]phenyl]methanesulfonamide **hemifumarate**, and artilide, the R-(+)-enantiomer of N-[4-[4-(di-n-butylamino)-1-hydroxybutyl]phenyl]methanesulfonamide **hemifumarate**, are under clin. investigation as Class III antiarrhythmic agents. For conducting drug disposition studies, the authors synthesized carbon-14 labeled ibutilide, as well as its two enantiomeric forms. In addition, high specific activity tritium labeled ibutilide was also prepared to facilitate development of RIA and for studying receptor site characteristics of this agent. Results of metabolism studies with [14C]ibutilide led the authors to prepare tritium labeled artilide, which is more readily accessible than the C-14 labeled drug. The optical antipode of artilide was also labeled with tritium for comparing drug disposition investigations on the two enantiomers.
AB Ibutilide **fumarate**, racemic N-[4-[4-(ethyl-n-heptylamino)-1-hydroxybutyl]phenyl]methanesulfonamide **hemifumarate**, and artilide, the R-(+)-enantiomer of N-[4-[4-(di-n-butylamino)-1-hydroxybutyl]phenyl]methanesulfonamide **hemifumarate**, are under clin. investigation as Class III antiarrhythmic agents. For conducting drug disposition studies, the authors synthesized carbon-14 labeled ibutilide, as well as its two enantiomeric forms. In addition, high specific activity tritium labeled ibutilide was also prepared to facilitate development of RIA and for studying receptor site characteristics of this agent. Results of metabolism studies with [14C]ibutilide led the authors to prepare tritium labeled artilide, which is more readily accessible than the C-14 labeled drug. The optical antipode of artilide was also labeled with tritium for comparing drug disposition investigations on the two enantiomers.

L14 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:62120 CAPLUS
DN 114:62120
TI Preparation of 3-(1-substituted-4-piperazinyl)-1H-indazoles as analgesics and antipsychotics
IN Strupczewski, Joseph T.; Bordeau, Kenneth J.
PA Hoechst-Roussel Pharmaceuticals, Inc., USA
SO U.S., 27 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4954503	A	19900904	US 1989-405161	19890911
	US 5077405	A	19911231	US 1990-526154	19900521
	EP 417653	A1	19910320	EP 1990-117251	19900907
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	CA 2024996	AA	19910312	CA 1990-2024996	19900910
	NO 9003925	A	19910312	NO 1990-3925	19900910
	AU 9062298	A1	19910314	AU 1990-62298	19900910
	ZA 9007174	A	19910626	ZA 1990-7174	19900910
	JP 03167175	A2	19910719	JP 1990-237300	19900910
PRAI	US 1989-405161		19890911		

OS CASREACT 114:62120; MARPAT 114:62120
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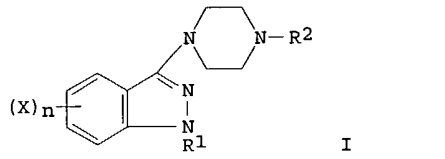

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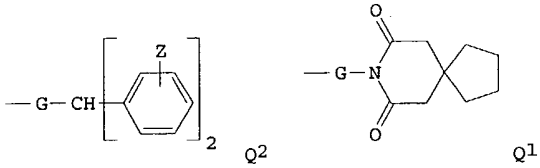
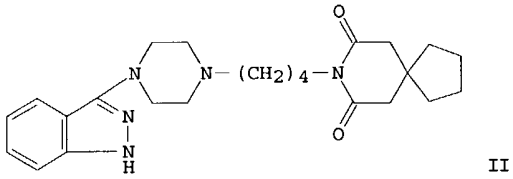


Q2 Q1



II

AB Title compds. I [R1 = H, (cycloalkyl- or aryl)alkyl, PhSO2; R2 = H, (hydroxy- or aryl- or cycloalkyl)alkyl, acyl, Q1, Q2 (G = lower alkylene, Z = H, halo, alkoxy, CF3, NO2, NH2), etc.; X = H, alkyl, OH, halo, alkoxy, CF3, NO2, NH2; n = 1-4; R2 ≠ alkyl when R1 = H or acyl and X = Cl], useful as analgesics and antipsychotics, were prepared For example, the **hemifumarate** of II was prepared in 17% yield by N-alkylation of 3-(1-piperazinyl)-1H-indazole, followed by acidification by **fumaric** acid. The s.c. ED50 for II-**hemifumarate** for inhibition of writhing in mice was 0.07 mg/kg, vs. 3.9 mg/kg for propoxyphene (std). The antipsychotic activity of II was also demonstrated by the apomorphine climbing assay in mice.

AB Title compds. I [R1 = H, (cycloalkyl- or aryl)alkyl, PhSO2; R2 = H, (hydroxy- or aryl- or cycloalkyl)alkyl, acyl, Q1, Q2 (G = lower alkylene, Z = H, halo, alkoxy, CF3, NO2, NH2), etc.; X = H, alkyl, OH, halo, alkoxy, CF3, NO2, NH2; n = 1-4; R2 ≠ alkyl when R1 = H or acyl and X = Cl], useful as analgesics and antipsychotics, were prepared For example, the **hemifumarate** of II was prepared in 17% yield by N-alkylation of 3-(1-piperazinyl)-1H-indazole, followed by acidification by **fumaric** acid. The s.c. ED50 for II-**hemifumarate** for inhibition of writhing in mice was 0.07 mg/kg, vs. 3.9 mg/kg for propoxyphene (std). The antipsychotic activity of II was also demonstrated by the apomorphine climbing assay in mice.

L14 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:630962 CAPLUS
DN 113:230962
TI Preparation of chalcone oxime ethers as 5-HT2 receptor antagonists and platelet antiaggregants
IN Congy, Christian; Labeeuw, Bernard; Gueule, Patrick; Rinaldi, Murielle
PA SANOFI, Fr.
SO Eur. Pat. Appl., 48 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 373998	A1	19900620	EP 1989-403339	19891201
	EP 373998	B1	19930811		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	FR 2639942	A1	19900608	FR 1988-15860	19881202
	FR 2639942	B1	19910329		
	AU 8945688	A1	19900607	AU 1989-45688	19891129
	AU 623706	B2	19920521		
	DK 8906059	A	19900603	DK 1989-6059	19891130
	DK 174434	B1	20030303		
	NO 8904786	A	19900605	NO 1989-4786	19891130
	NO 171269	B	19921109		
	NO 171269	C	19930217		
	CA 2004350	AA	19900602	CA 1989-2004350	19891201

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	CA 2004350	C	19970603		
	ZA 8909201	A	19900926	ZA 1989-9201	19891201
	JP 02262552	A2	19901025	JP 1989-313121	19891201
	JP 2562503	B2	19961211		
	US 5166416	A	19921124	US 1989-444823	19891201
	AT 92914	E	19930815	AT 1989-403339	19891201
	IL 92519	A1	19940530	IL 1989-92519	19891201
	ES 2059804	T3	19941116	ES 1989-403339	19891201
	FI 94752	B	19950714	FI 1989-5757	19891201
	FI 94752	C	19951025		
	AU 9212183	A1	19920528	AU 1992-12183	19920310
	AU 640310	B2	19930819		
	US 5290951	A	19940301	US 1992-911736	19920710
PRAI	FR 1988-15860	A	19881202		
	EP 1989-403339	A	19891201		
	US 1989-444823	A3	19891201		

OS MARPAT 113:230962

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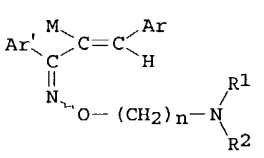

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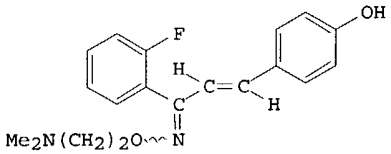

II

AB Title ethers I [Ar, Ar' = (substituted) Ph, 9-anthryl, naphthyl, pyridyl, thienyl, furyl; R1, R2 = H, alkyl; or NR1R2 = pyrrolidino, piperidino, morpholino, were prepared as 5-HT2 receptor antagonists and platelet antiaggregants (no data). For example, condensation of 2-FC6H4Ac with 4-MeOC6H4CHO in HCl-EtOH and demethylation of the product with BBr3 gave 2-FC6H4COCH:CHC6H4OH-4, which was further condensed with Me2N(CH2)2ONH2 in HCl-EtOH with alkaline workup (pH >8) to give title ether II as a 45:55 syn/anti mixture Treatment of the mixture with **fumaric** acid in EtOH gave crystalline syn-II **hemifumarate.** Eighty-eight synthetic examples are given.

AB Title ethers I [Ar, Ar' = (substituted) Ph, 9-anthryl, naphthyl, pyridyl, thienyl, furyl; R1, R2 = H, alkyl; or NR1R2 = pyrrolidino, piperidino, morpholino, were prepared as 5-HT2 receptor antagonists and platelet antiaggregants (no data). For example, condensation of 2-FC6H4Ac with 4-MeOC6H4CHO in HCl-EtOH and demethylation of the product with BBr3 gave 2-FC6H4COCH:CHC6H4OH-4, which was further condensed with Me2N(CH2)2ONH2 in HCl-EtOH with alkaline workup (pH >8) to give title ether II as a 45:55 syn/anti mixture Treatment of the mixture with **fumaric** acid in EtOH gave crystalline syn-II **hemifumarate.** Eighty-eight synthetic examples are given.

L14 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1990:76638 CAPLUS

DN 112:76638

TI Preparation of phenylacetonitriles as α-blockers

IN Ito, Yasuo; Kato, Hideo; Etsuchu, Eiichi; Ogawa, Nobuo; Mitani, Kazuya; Sakurai, Shunichiro

PA Hokuriku Pharmaceutical Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 01190660	A2	19890731	JP 1988-13585	19880126
PRAI	JP 1988-13585		19880126		

OS MARPAT 112:76638

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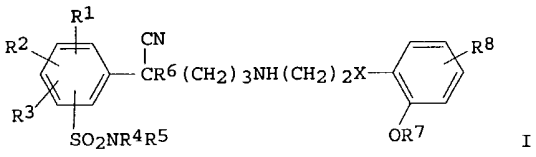

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AB Title compds. I [R1, R2, R3 = H, lower alkoxy; R4, R5 = H, lower alkyl, R4R5N maybe (un)substituted (hetero-containing) four- to seven-membered ring; R6 = linear or branched C1-8 alkyl; R7 = lower alkyl; R8 = H, halo; X = O, S] and their pharmacol. acceptable salts, useful for treatment of hypertension and dysuria (no data), are prepared α-Isopropyl-4-methoxyphenylacetonitrile in THF was treated with BuLi in hexane at 0° for 30 min and then with 1-bromo-3-chloropropane at 0° for 30 min to give α-(3-chloropropyl)-α-isopropyl-4-methoxyphenylacetonitrile (II). II was refluxed with HSO3Cl in CH2Cl2 for 1.5 h, treated with H2O, extracted with CHCl3, concentrated, and the residue was treated with ammonia at 0° for 1.5 h to afford α-(3-chloropropy)-α-isopropyl-4-methoxy-3-sulfamoylphenylacetonitrile (III). III was treated with 2-(2-methoxyphenoxy)ethylamine at 95° for 4.5 h, acidified with 10% HCl, extracted, concentrated, and the residue was treated with **fumaric** acid to give α-isopropyl-4-methoxy-α-[3-[2-(methoxyphenoxy)ethylamino]propyl]-3-sulfamoylphenylacetonitrile **hemifumarate.**

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